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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/672,949	09/26/2003	Jamie Marie Davis	PC25413A	9410

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WARNER-LAMBERT COMPANY
2800 PLYMOUTH RD
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EXAMINER

BERNHARDT, EMILY B

ART UNIT PAPER NUMBER

1624

DATE MAILED: 10/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/672,949	Applicant(s) DAVIS ET AL.	
	Examiner Emily Bernhardt	Art Unit 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-17 is/are pending in the application.
 4a) Of the above claim(s) 9-17 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-8 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>12/01/03</u> . | 6) <input type="checkbox"/> Other: ____. |

Restriction to one of the following inventions is required under 35 U.S.C.

121:

- I. Claims 1-8, drawn to compounds, simple compositions where $Y=N$, classified in class 544, subclasses 361,363 and many other subclasses based on nature of Ar and Q ring; class 514 subclasses 253.03, 253.07, etc.
- II. Claims 1 and 8, drawn to compounds, simple compositions where $Y=CH$, classified in class 546, subclasses 157-158 and class 544 various subclasses based on Ar and Q ring; class 514 subclass 312,etc.
- III. Claims 9-15, drawn to multiple uses employing compounds of I, classified in class 514, subclass 253.03,etc.
- IV. Claims 9-15, drawn to multiple uses employing compounds of II, classified in class 514, subclass 312,etc.
- V. Claims 16-17, drawn to multiple uses employing compounds of I and additional active ingredients, classified in class 514, subclasses various as determined by the exact nature of ingredients employed.
- VI. Claims 16-17, drawn to multiple uses employing compounds of II and additional active ingredients, classified in class 514, subclasses various as determined by the exact nature of ingredients employed.

If one of Groups III or IV is elected applicants must pick a single use.

If V or VI is elected applicants must pick a single use and an ultimate species pair of active ingredients. If I-IV is elected an ultimate species is also needed .

The inventions are distinct, each from the other because of the following reasons: Compounds within groups I-II relate to compounds of considerable structural dissimilarity in view of the varying central core as well as ring systems permitted at either end of the azine core. Thus they are separately and variously classified. Each can support a patent as the compounds of each group are capable of being utilized alone not in combination with other members listed in the Markush group and are not art-recognized equivalents.

Inventions I/II and III/IV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the

instant case a variety of uses are urged for the compounds of the invention which may separate issues from an examination of just the compound/composition claims.

Additionally, compounds employed in I-II may be old or obvious for a particular use when separately employed but may be patentable due to superior, or synergistic properties not present for the individual components in I-II. Within groups V-VI there is more than one invention as the claims embrace multiple combinations for a variety of uses which require independent searches and which are not art-recognized equivalents in the art.

During a telephone conversation with Ms. Harvey on 9/26/05 a provisional election was made with traverse to prosecute the invention of I, claims 1-8 and in particular species of eg.3. Affirmation of this election must be made by applicant in replying to this Office action. Claims 9-15 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are

governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

In view of the many differing permutations present within Ar as well as Q ring which are variously classified as set forth above, based on species elected (eg.3), corresponding "Ar" ring of Formula 1A with Q ring being 6-membered and

only containing 1 N and substituted, fused derivatives thereof will be held as constructively elected. The claims which read on this subject matter are: 1-8.

Applicants are advised that the claims will only be examined with respect to this elected subject matter.

The disclosure is objected to because of the following informalities: Parent history is missing identifying earlier provisional application. Note MPEP 1302.04.

Appropriate correction is required.

Claims 1,2,4,5,7 and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. "Preferably" in the Ar, Q, R1 and R5-R8 choices renders the scope unclear as to what is being claimed- subject matter before or after the term.

2. Oxo as a substituent on heteroaryl moieties makes no sense since doubly-bonded moieties as oxo would exceed valency requirements in such systems which are alternately doubly bonded.

3. The plethora of intended uses present in the composition claim 8 renders the intended "amount" ambiguous since it is not conceivable that the dosage regimens for uses as varied as depression vs neurodegenerative disorders vs.

addictive disorders would all be the same and there is nothing in the specification pointing to a particular regimen for the many recited uses. It is suggested that the uses be deleted since only one use is needed to support such a claim for compliance with 35 USC 112 and 101. See last paragraph of MPEP 2164.01(c), May 2, 2004 edition.

Claims 1-2,4,5,7-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

1. Starting material sources for the polycyclic rings resulting from one of R5-R8 joining with another of R5-R8 and spiro fusion permitted at these variables as well as in Q are not seen but are required. Specification is silent as to the availability of necessary reactants needed to prepare such ring systems of if they are commercially available. Note In re Howarth 210 USPQ 689; Ex parte Moersch 104 USPQ 122 for the need to show starting material sources commensurate with the claims' scope. The only other polycyclo ring systems are those corresponding to ortho fusion resulting in a cyclopentane ring (eg.32) and peri fusion resulting in a benzene ring as shown in eg.36.

2. As there are no such other polycyclic compounds that have been made corresponding to the instant scope which include carbo- and heterofused rings having 3 to 7 members and all degrees of unsaturation, there is no reasonable basis for assuming that the myriad of compounds embraced by the all the generic claims will all share the same physiological properties since they are so structurally dissimilar as to be chemically non-equivalent and there is no basis in the prior art for assuming the same. The same applies for the scope of substituents permitted on the Q ring system which includes heteroaryls which can be monocyclic, bicyclic and further substituted with more groups. Note *In re Surrey* 151 USPQ 724 regarding sufficiency of disclosure for a Markush group. Also see MPEP 2164.03 for enablement requirements in cases directed to structure-sensitive arts such as the pharmaceutical art. $\mu\mu$

Also note the criteria for enablement as set out in *In re Wands* cited in MPEP 2164.01(a), August 2000 edition, which includes factors such as:

1) Breadth of the claims- the claims cover compounds easily in the millions as pointed out above;

2) Level of unpredictability in the art- the invention is pharmaceutical in nature as it involves binding to serotonin (5HT_{2A}) and dopamine (D₂) receptors. It is well established that “the scope of enablement varies inversely with the degree

of unpredictability of the factors involved” and physiological activity is generally considered to be unpredictable. See *In re Fisher* 166 USPQ 18. A range of K_i values is reported which is enormous- covering $\leq 1\mu\text{M}$ to $.04\text{nM}$ - a 25000 fold spread;

3) Direction or guidance- as stated above the compounds made are not representative of the instant scope but are closer to each other than to remaining scope being mainly substituted with alkyl groups on a **quinolinone** ring

4) State of the prior art- The compounds are piperazine derivatives with benzofused rings at one end and a bicyclic 6-membered N- containing ring system connected via alkylene, etc. at the other end as well as fused derivatives thereof with substitution permitted at various ring positions. While such compounds are known as evident from the art applied below, they are similar in structure to the compounds made herein and thus do not evidence the many structural permutations permitted in the instant scope are known for at least one use in the prior art;

5) Working examples- Actual test data has been presented for 3 compounds and a range reported ($\leq 1\mu\text{M}$) for other undisclosed compounds and thus no clear evaluation of which functional groups at various positions out of the many claimed might affect potency to a large or small degree.

In view of the above considerations, this rejection is being applied.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Howard (EP'435) Howard describes very similar compounds to that claimed herein for use in treating psychosis and anxiety. See quinolinone species on p.3 and the working examples including examples 44 and 45. Said compounds differ from that claimed herein only in point of attachment to the quinolinone ring system- i.e. at the 6-position in Howard vs. 8-position herein. . Compounds that are position isomers are expected to have similar properties. See for example In re Crounse 150 USPQ 554; Ex parte Engelhardt 208 USPQ 343; In re Mehta 146 USPQ 284; In re Norris 84 USPQ 458 and MPEP 2144.09 (2/03 Edition) regarding position isomerism. Thus it would have been obvious at the time the invention was made to expect instant compounds to possess the utility taught by the applied art in view of the close structural similarity outlined above.

Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Andreanna (US'230). The commonly assigned patent publication is applied as of its earliest 119(e) filing date which preceded applicants' earliest priority date. It

describes very similar compounds with the sole difference being the point of attachment to the quinolinone ring system- i.e. at the 6-position in US'230 vs. 8-position herein. Thus they are obvious variants for the same reason as discussed in the above 103 rejection over Howard.

While evidence of common ownership is now enough to disqualify commonly assigned art under 103 based on 102(e) as well as 102(f) or (g) in view of the passage of the American Inventors Protection Act, there must be provided a clear statement by applicants, attorney or agent of record that instant application and US'143 at the time the instant invention was made were commonly owned. See 1241 OG 96, December 26, 2000.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-8 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 of copending Application No. 10/660908. Although the conflicting claims are not identical, they are not patentably distinct from each other because they embrace subject matter that are obvious variant as discussed in the above 103 rejection. Note that avoidance of literal overlap is not enough to preclude an obviousness-type double patenting rejection. See MPEP 804, section on "Obvious-type".

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned 10/660908, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Bernhardt whose telephone number is 571-272-0664.

If attempts to reach the examiner by telephone are unsuccessful, the acting supervisor for AU 1624, James O. Wilson can be reached at 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.



Emily Bernhardt
Primary Examiner
Art Unit 1624